After the claims, insert the substitute amended Abstract of the Disclosure, with is attached hereto.

In the Claims:

Please amend claims 16, 17-20, 22, 26, 28-30, 38 and 39 as follows:

16. (Amended) A polyketide synthase (PKS) multienzyme for use in producing a polyketide having substantially exclusively a desired starter unit, said PKS multienzyme comprising a loading module and a plurality of extension modules, wherein said loading module is adapted to load an optionally substituted malonyl and then to effect decarboxylation of the loaded residue to provide a corresponding optionally substituted acetyl residue for transfer to an adjacent one of said extension modules, and wherein at least one of the extension modules is not naturally associated with a loading module that effects decarboxylation; with the proviso that the polyketide produced by the polyketide synthase is not a 14-membered macrolide having a 13-methyl group due to incorporation of an unsubstituted acetate starter; said multienzyme having the ability to synthesize said polyketide produced by the polyketide synthase.

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17. (Amended) A type I polyketide synthase which comprises a loading module and a plurality of extension modules, wherein said loading module is adapted to load an optionally substituted malonyl and then to effect decarboxylation of the loaded residue to provide a corresponding optionally substituted acetyl residue for transfer to the first of said extension modules, and wherein at least said first extension module is not naturally associated with a loading module that effects decarboxylation; with the proviso that (a) the synthase is not composed of the loading module of the tylosin polyketide synthase coupled to the spiramycin polyketide synthase minus its natural loading module; and (b) the polyketide produced by the polyketide synthase is not a 14-membered macrolide having a 13-methyl group due to incorporation of an unsubstituted acetate starter unit.

18. (Amended) A synthase according to claim 17, wherein the decarboxylating functionality of the loading module is provided by a ketosynthase (KS)-type domain which differs from a KS domain of an extension module by having a glutamine residue in place of cysteine in the active site.

19. (Amended) A synthase according to claim 17, wherein the decarboxylating functionality of the loading module is provided by a polypeptide of the type which is

alternatively designated as chain length factor (CLF) or ketosynthase (KS) β domain.

20. (Amended) A synthase according to claim 17, wherein the loading module's loading functionality is provided by an acyltransferase-type domain having an arginine residue in the active site.

22. (Amended) A type I polyketide synthase according to claim 17, wherein the loading and decarboxylating functionality is provided by a KSq-Atq pair derived from a ketosynthase (KS)-acyltransferase (AT) pair of domains which naturally occur together in an extension module wherein KSq represents the N-terminal ketosynthase-like domain of a loading module in which there is a glutamine residue in place of the active site cysteine residue of a KS domain of an extension module which is essential for beta-ketoacyl-ACP synthase activity and wherein ATq represents an AT domain as found immediately C-terminal of a KSq domain.

26. (Amended) A type I polyketide synthase according to claim 20, wherein said acyltransferase domain corresponds to the acyltransferase of module 6 of the neddamycin polyketide synthase.

28. (Amended) A synthase according to claim 17, wherein the loading module includes an acyl carrier protein.

29. (Amended) A synthase according to claim 17, wherein at least the KSq domain of said loading module corresponds to the KSq domain of the loading module of the PKS multienzyme of oleandomycin, spiramycin, niddamycin, methymycin, tylosin or monensin wherein KSq represents the N-terminal ketosynthase-like domain of a loading module in which there is a glutamine residue in place of the active site cysteine residue of a KS domain of an extension module which is essential for beta-ketoacyl-ACP synthase activity.

30. (Amended) A type I polyketide synthase according to claim 17, wherein said polyketide synthase is adapted to synthesize a polyketide selected from

(a) 12- and 16-membered macrolides with acetate starter units;

(b) 12, 14 and 16-membered macrolides with propionate starter units;

(c) variants of rifamycin, avermectin, rapamycin, immunomycin and FK506 with acetate starter units or propionate starter units; or

(d) a polyketide wherein the starter unit gave rise to a sidechain selected from allyl and hydroxymethyl.

38. (Amended) A type I polyketide synthase which comprises a loading module and a plurality of extension modules, wherein said loading module is adapted to load an optionally substituted malonyl and then to effect decarboxylation of the loaded residue to provide a corresponding optionally substituted acetyl residue for transfer to the first extension module, and wherein at least part of the first extension module is heterologous to said loading module or at least a domain thereof; with the proviso that (a) the synthase is not composed of the loading module of the tylosin polyketide synthase coupled to the spiramycin polyketide synthase minus its natural loading module; and (b) the synthase is not adapted to direct the synthesis of a 14-membered macrolide having a 13-methyl group due to incorporation of an unsubstituted acetate starter unit.

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39. (Amended) A type I polyketide synthase enzyme or part thereof comprising a loading module of the form:

(decarbox) (AT) (ACP) where (ACP) represents an acyl carrier protein

(AT) represents an acyltransferase domain operative to load selectively a substrate selected from optionally substituted malonate units onto the ACP, and

(decarbox) represents a domain operative to decarboxylate an optionally substituted malonate substrate carried by the

ACP, the (decarbox) being selected from a KSq domain and a polypeptide of the type which is alternatively designated as chain length factor (CLF) or ketosynthase (KS) β domain; wherein the loading module includes domains or portions thereof derived from different sources and/or comprises engineered domains wherein KSq represents the N-terminal ketosynthase-like domain of a loading module in which there is a glutamine residue in place of the active site cysteine residue of a KS domain of an extension module which is essential for beta-ketoacyl-ACP synthase activity.

C21 CONT

Marked-up versions of the present amendments to specification pages 32, 33, 43, 47, 49, 53, 58, 59, 63, 64, 70 and 72 and claims 16, 17-20, 22, 26, 28-30, 38 and 39 are submitted herewith.

Please add the following new claims:

41. (New) A genetically engineered type II polyketide synthase (PKS) which differs from the wild-type PKS in that the wild-type PKS includes a domain of the type alternatively designated as chain length factor ("CLF") or ketosynthase (KS) β which has decarboxylating activity, and said activity is suppressed in the genetically engineered type II PKS.

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42. (New) A genetically engineered type II PKS according to claim 41 which differs from the wild-type PKS in that the wild-type PKS has a Gln residue in the decarboxylation active site of said domain which is replaced by a different residue in said genetically engineered PKS.

43. (New) A type I polyketide synthase which comprises a loading module and a plurality of extension modules, wherein said loading module is adapted to load an optionally substituted malonyl and then to effect decarboxylation of the loaded residue to provide a corresponding optionally substituted acetyl residue for transfer to the first of said extension modules, and wherein said loading module is of the form:

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(Dec)-(AT)-(ACP)

wherein ACP represents an acyl carrier protein domain, AT represents an acyltransferase domain which is adapted to load an optionally substituted malonyl; and Dec represents a domain which is adapted to effect decarboxylation of a loaded optionally substituted malonyl; wherein at least one of the domains is heterologous to other domains of the loading module or is an engineered domain.

✓ Cancel claims 31-37.